MicroRNA let-7b regulates neural stem cell proliferation and differentiation by targeting nuclear receptor TLX signaling.

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Public Summary:

Scientific Abstract:
Neural stem cell self-renewal and differentiation is orchestrated by precise control of gene expression involving nuclear receptor TLX. Let-7b, a member of the let-7 microRNA family, is expressed in mammalian brains and exhibits increased expression during neural differentiation. However, the role of let-7b in neural stem cell proliferation and differentiation remains unknown. Here we show that let-7b regulates neural stem cell proliferation and differentiation by targeting the stem cell regulator TLX and the cell cycle regulator cyclin D1. Overexpression of let-7b led to reduced neural stem cell proliferation and increased neural differentiation, whereas antisense knockdown of let-7b resulted in enhanced proliferation of neural stem cells. Moreover, in utero electroporation of let-7b to embryonic mouse brains led to reduced cell cycle progression in neural stem cells. Introducing an expression vector of Tlx or cyclin D1 that lacks the let-7b recognition site rescued let-7b-induced proliferation deficiency, suggesting that both TLX and cyclin D1 are important targets for let-7b-mediated regulation of neural stem cell proliferation. Let-7b, by targeting TLX and cyclin D1, establishes an efficient strategy to control neural stem cell proliferation and differentiation.

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